Topical 10% Tranexamic Acid for Recalcitrant Topical Steroid-Dependent Face

Sir,

Topical steroid dependent/damaged face (TSDF) is defined as a semi-permanent or permanent damage to the skin of the face precipitated by the irrational, indiscriminate, unsupervised, or prolonged use of topical corticosteroids (TC) resulting in a plethora of cutaneous signs and symptoms and psychological dependence on the drug.[1] Once damaged, the management becomes challenging as the treatment options are very limited and results are unpredictable. We present a case of recalcitrant TSDF with excellent response to topical 10% tranexamic acid (TXA).

A 21-year-old girl (Fitzpatrick type IV-V) presented with persistent erythema of the face with associated itching and burning sensation [Figure 1a and b]. On enquiring, she gave history of application of betamethasone dipropionate cream twice daily for past 5 months. She was advised by a local pharmacist to apply betamethasone dipropionate cream for her freckles. Since last 1 month, she has been experiencing a burning sensation on face and a persistent erythema. Patient was asked to stop the topical steroid application and was advised strict photoprotection. Topical tacrolimus 0.1% was prescribed at nighttime but was discontinued after 8 weeks due to minimal improvement of symptoms. Topical brimonidine 0.33% was given later, which showed initial improvement. The lesions, however, reappeared on discontinuation of therapy. Patient was then started on topical 10% TXA, which was prepared from injection TXA (100 mg/ml). The solution was dispensed in an ethylene/propylene copolymer plastic container and patient was educated to apply it with a cotton bud once daily at night. In addition, a physical sunscreen was also advised. Burning sensation decreased within 2 weeks. Erythema was assessed using a clinician erythema assessment scale[2] [Table 1] and it showed a 2-grade reduction (baseline grade-4) after 4 weeks [Figure 2a and b]. Treatment was continued till 8 weeks, after which it was stopped and patient was asked to continue using the sunscreen. There was no relapse in the next 4 weeks, after which the patient was lost to follow up.

The clinical picture of TSDF appears due to a combination of factors: dermal atrophy (TC inhibit collagen and hyaluronic acid synthesis by fibroblasts),[3] local immunosuppression, and inhibition of action of nitric oxide (NO).[4,5] On withdrawal of TC, endothelial NO is released causing vasodilation and erythema.[4,5]

TXA is a synthetic lysine-like molecule, which competitively inhibits the conversion of plasminogen into plasmin, thereby inhibiting the plasmin mediated angiogenesis.[2] In addition, it is known to inhibit vascular endothelial growth factor. Topical TXA has been used in the management of rosacea.[2,3] Tranexamic acid decreases the clinical signs of rosacea via inhibition of PAR-2 activation by serine protease and calcium influx in keratinocytes.[2] Additionally, it decreases erythema by decreasing pro-inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha).[3]

Treatment of TSDF includes withdrawal of the topical corticosteroid, which itself can lead to the increased flushing and erythema due to released nitric oxide from the endothelia.[4,5] Oral anti-inflammatory antibiotics, topical

Table 1: Clinician erythema assessment scale description

Grade 1	CEA scale description
0	Clear skin with no signs of erythema
1	Almost clear, slight redness
2	Mild erythema, definite redness
3	Moderate erythema, marked redness
4	Severe erythema, fiery redness

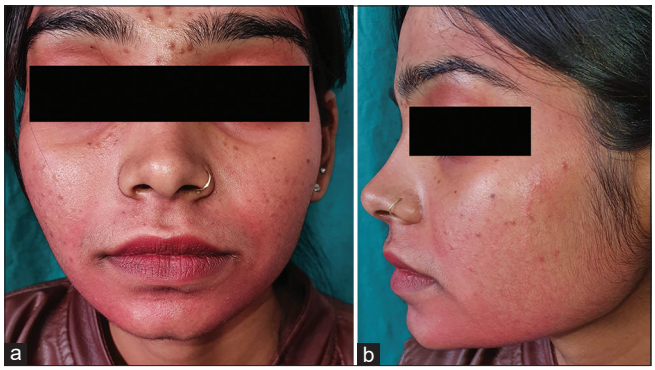

Figure 1: Dusky erythema over the face of a young girl (a); lateral view showing topical steroid induced erythema (b)

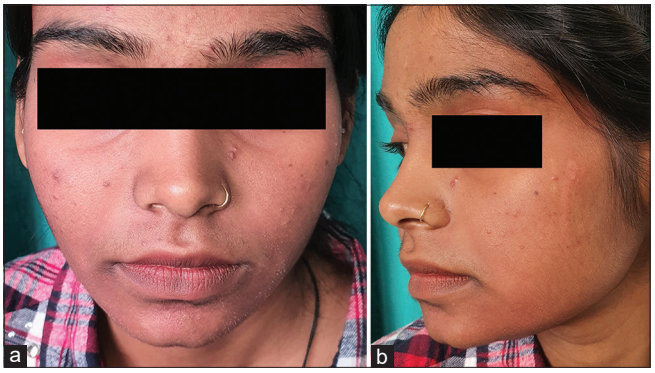

Figure 2: Improvement of the erythema after 4 weeks of topical 10% tranexamic acid application (a); lateral view showing improvement in erythema (b)

Table 2: Topical therapeutic modalities for topical steroid dependent face

Topical therapeutic modality	Mechanism of action
Topical tacrolimus/pimecrolimus	Calcineurin antagonist that causes immunosuppression and anti-inflammatory effect by blocking T-cell activation, thereby down-regulating interleukin (IL)-2, IL-4, IL-10, and other cytokine.
Topical brimonidine	Alpha-adrenoceptor agonist and causes vascoconstriction of cutaneous microcirculation
Topical xylometazoline	Alpha-adrenoceptor agonist and causes vasoconstriction of cutaneous microcirculation
Topical metronidazole	Anti-inflammatory effect that interferes with neutrophil release of reactive oxygen species
Topical azelaic acid	Anti-inflammatory effect through inhibition of the production of reactive proinflammatory oxygen species (hydroxy and super oxyradicals) from neutrophils.
Topical ivermectin	Inhibit the innate inflammatory cascade by inhibiting demodex (which may increase due to immunosuppressive action of topical corticosteroids)
Topical clindamycin	Reduces bacterial superantigens that proliferate due to immunosuppressive action of topical corticosteroids, in addition to having anti-inflammatory properties
Sunscreen	Protects against the Ultraviolet light damage and reduces trans-epidermal water loss.
Topical tranexamic acid	Inhibits the conversion of plasminogen into plasmin, thereby inhibiting the plasmin mediated angiogenesis. In addition it inhibits vascular endothelial growth factor. It also causes inhibition of PAR-2 activation by serine protease and calcium influx in keratinocytes. Lastly, it decreases erythema by decreasing pro-inflammatory cytokines (interleukin 6 and tumor necrosis factor alpha)

metronidazole, topical tacrolimus/pimecrolimus, topical brimonidine, and topical xylometazoline has been used in past with variable results [Table 2].[2] Increasing evidence of TXA in the reduction of erythema prompted us to start the patient on 10% TXA.[6-9] Commercially, TXA preparation as solo therapeutic agent is not available and hence has to be prepared from the injectable form. The preparation has to be stored in an ethylene/propylene plastic bottle. The preparation should be stored away from light and at room temperature.[8,9]

Dryness was the only side-effect reported by our patient during the therapy. A moisturizer was prescribed to deal with dryness. A long-term follow-up could not be done in our patient, which is the limitation of this report. Our report shows a promising role of TXA in TSDF. However, further studies with increased sample size and long-term follow-up is needed to conclude the role of TXA in the management of TSDF.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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